REMARKS

Entry of the present amendment and reconsideration of this Application is respectfully requested. Claims 71-82 and 84 are amended herein. These amendments introduce no new matter, and their entry is respectfully requested. After entry of the present Amendment, claims 18, 71-82, and 84 are pending in the application and under examination.

The amendments to claims 71-82 and 84 are to correct a grammatical error and to clarify the claim language. These amendments add no new matter, and their entry is respectfully requested. Based on the above amendments and the following remarks, applicant respectfully requests that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Claim Rejections under 35 U.S.C. § 112

Claims 18, 71-82, and 84 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants have amended claims 18, 71-82, and 84 herein to clarify that the first microarray being contacted in step (a) of claim 18 is referred to in dependent claims and to correct the grammatical error in which "claims" rather than "claim" was recited. Accordingly, Applicants respectfully request removal of the rejection of claims 18, 71-82, and 84 under 35 U.S.C. § 112, second paragraph.

Claim Rejections under 35 U.S.C. §103(a)

Ekins et al. (Clin. Chem. 37: 1955-1967) and Yates III et al. (U.S. Patent 5,538,897)

Claims 18, 71-75 have been rejected under 35 U.S.C. §103(a) as allegedly being obvious over Ekins et al. in view of Yates III, et al.. Applicants respectfully traverse this rejection for at least the following reasons.

The MPEP states that to establish a prima facie case of obviousness there must be some suggestion or motivation in the prior art to make the claimed invention, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all of the claim limitations. MPEP § 2142; In re Vaeck, 947 F.2d 488, 20 USPQ2d, 1438 (Fed. Cir. 1991).

The reference teachings must be sufficient for one of ordinary skill in the relevant art having the reference before him or her to make the proposed substitution, combination, or other modification. In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972). MPEP 2143.01. Further, in making a rejection based on obviousness, the Examiner must consider the invention as a whole. Bausch & Lomb v. Barnes-Hind/Hydrocurve, Inc., 796 F.2d 443, 447-49, 230 USPQ 416, 419-20 (Fed. Cir. 1986), cert. denied, 484 U.S. 823 (1987). MPEP 2141.02.

In the first place, Applicants respectfully assert that the references cited in the rejection fail to disclose all of the claim limitations. Ekins et al. describe the development of a microspot immunoassay of high sensitivity. Yates III, et al. disclose methods of identifying peptides using tandem mass spectrometry and comparing the mass of the fragmented peptides with a database of peptides of known sequence (from which their molecular weight is calculated), combined with statistical best fit analysis. Neither Ekins et al. nor Yates III, et al. disclose 1) a binding pattern resulting from contacting a cell lysate with a microarray of antibodies; 2) comparing the binding pattern generated using a cell lysate of a first cell population with the binding pattern generated using a cell lysate of a second cell population; or, 3) identification of proteins that are differentially expressed in two cell populations by comparing binding patterns, as recited in Claim 18.

Ekins et al. nowhere disclose a binding pattern, a cell lyate, or a binding pattern resulting from contact of a cell lysate with antibodies. Rather, Ekins et al. describe the development of a quantitative immunoassay based on spotted antibodies, and compare the sensitivity of a microspot assay combined with detection using confocal microscopy with other types of immunoassays. Applicants dispute the notation in the Office Action of October 25, 2006 that indicates Figures 4 and 5 of Ekins et al. depict "monitoring the expression and properties of a large number of proteins". In fact, Figure 4 of Ekins et al. schematically depicts the binding of a single analyte to a single species of immobilized antibody, showing pictorially that a fraction of the antibody sites are occupied by the analyte. Figure 5 of Ekins schematically illustrates competitive and noncompetitive immunoassays, in which, as in Figure 4, each illustration of immobilized antibodies represents antibodies with affinity for a single analyte. Applicants further disagree that Figure 8 of Ekins et al. depicts the comparison of microspot assay devices, as alleged in the Office Action. Rather, the figure shows sequentially the assay procedure, with the

two branches of the right panel indicating alternative detection methods: The left panel of Figure 8 depicts an immobilized antibody "spot" comprising multiple antibody molecules reactive against a single analyte incubated with a test sample (within rectangle) followed by removal of the sample and washing of the device to provide an immobilized antibody spot having fractional occupancy of the antibody binding sites. The right panel of Figure 8 shows the next stage of the detection procedure, which can be performed alternatively as 1) a noncompetitive assay in which the immobilized antibody spot having fractional occupancy of the antibody binding sites is incubated with (labeled) anti-analyte antibody (arrow pointing downward on the left) or 2) a competitive assay in which the immobilized antibody spot having fractional occupancy of the antibody binding sites is incubated with (labeled) anti-idiotypic antibody (arrow pointing downward on the right). Figure 8 thus depicts alternative strategies for detection and does *not* compare microspot assay devices. Applicants do agree, however, with the statement of the Office Action that Ekins et al. does not teach the generation of binding patterns for comparison.

Applicants disagree, however, with the statement in the pending Office Action that Yates III, et al. disclose the evaluation of binding patterns to identify peptide amino acid sequences. Applicants find no statement to that effect in the abstract, nor are Applicants aware of any disclosure of "binding patterns" anywhere in the specification of Yates III, et al. Rather, Yates III, et al. teach performing tandem mass spectrometry (MS/MS) on protease digested samples, and comparing the resulting mass spectra of protein fragments and their subfragments to predicted mass spectra (or mass calculations of protein fragments and subfragments) of proteins based on their sequences in databases of protein or nucleic acid sequences. No binding pattern is found in Yates III, et al.

The Office Action states: "Antibody-protein binding is employed to measure cellular proteins (resting state – normal state)." Applicants disagree with this characterization of the teaching of Yates III, et al. Yates III, et al. teach determining the mass (or molecular weight) of peptides using mass spectrometry in order to identify the proteins from which the peptides are derived, but this is unrelated to the subject matter of the claims. The Office Action goes on to state, in referring to disclosure in Yates III, et al.: "The protein pattern or fragment is stored and compared with database patterns to determine diseases and/or disorders (stimulated state)." Applicants stress that the use of

the word "pattern" by Yates III, et al. refers to the mass spectra of a protein fragment and its subfragments. It is not, as recited in independent Claim 18, a binding pattern generated by contacting a cell lysate with a microarray of antibodies, nor is it a protein-antibody binding pattern, *nor is it a binding pattern of any type*.

The pending Office Action acknowledges that the references are silent with respect to the cell proteins being evaluated in a cell lysate (page 6 of the Office Action). However, it is then stated that "absent evidence to the contrary . . . Yates III, et al. read on cell lysates because they teach protein digestion of lysing [sic] for determination." Applicants respectfully point out that Claim 18 requires not that a cell lysate be used for isolating proteins to be digested for determining peptide sequences using mass spectrometry, but rather Claim 18 recites that a cell lysate be contacted with a microarray of antibodies on a solid support to generate a binding pattern. This is not taught in Yates III et al., nor is contacting a lysate with a microarray of antibodies taught in Ekins et al. Thus the cited references do not include, alone or in combination, all elements of independent Claim 18.

The Office Action also fails to establish a prima facie case of obviousness in that no suggestion or motivation is provided to combine the references to make the claimed invention is provided. Yates III, et al. and Ekins et al. do not, in themselves or together, suggest generating a binding pattern by contacting an antibody microarray with a cell lysate, and certainly provide no motivation for doing so. Yates III, et al. and Ekins et al. are concerned with identification of proteins or the detection of analytes in samples; however, neither reference bears on comparison of cell populations, or identifying proteins that are differentially expressed in different cell populations. Applicants strongly disagree that, as alleged in the Office Action (bottom of page 6), Yates III, et al. "taught that binding patterns could not only identify disease and or disorders but could further identify the sequence or sub-sequences of the proteins/peptides involved." Yates III, et al. do not teach, disclose, or suggest binding patterns of any kind, and do not motivate one of average skill in the art to generate binding patterns of any type, or motivate comparison of binding patterns of different cell types.

Thus, all limitations of the rejected claims are not present in the cites references, and the references do not provide a suggestion or motivation to make the claimed invention as required

for a prima facie case of obviousness under 35 U.S.C. §103(a). Applicants assert that independent Claim 18 and Claims 71-75 that depend from Claim 18 are nonobvious under 35 U.S.C. §103(a), and Applicants respectfully request that the rejection be withdrawn.

Ekins et al. (Clin. Chem. 37: 1955-1967) and Yates III et al. (U.S. Patent 5,538,897); and Cupo (J. Chromatography 569: 389-400 (1991))

Claims 76-79 and 84 have been rejected under 35 U.S.C. §103(a) as being unpatentable of over Ekins et al., Yates III et al., and further in view of Cupo. Applicants respectfully traverse this rejection. Claims 76-79 and 84 depend from Claim 18. As argued above in traversing the rejection of Claim 18, Ekins et al. and Yates III, et al. do not disclose binding patterns. Cupo does not make up for the deficiencies of Ekins et al and Yates III, et al., in that Cupo also does not disclose or suggest binding patterns generated by contacting a microarray of antibodies with a cell lysate. Thus, Claims 76-79 and 84 are nonobvious for the same reason that claim 18 is nonobvious, and Applicants respectfully request that the rejection be removed.

Ekins et al. (Clin. Chem. 37: 1955-1967) and Yates III et al. (U.S. Patent 5,538,897); and Spencer et al. (WO 93/12248)

Claims 76-79 and 84 have been rejected under 35 U.S.C. §103(a) as being unpatentable of over Ekins et al., Yates III et al., and further in view of Spencer et al. Applicants respectfully traverse this rejection. Claims 80-82 depend from Claim 18. As argued above in traversing the rejection of Claim 18, Ekins et al. and Yates III, et al. do not disclose binding patterns, and in particular do not disclose binding patterns generated by contacting a microarray of antibodies with a cell lysate. Spencer does not make up for the deficiencies of Ekins et al and Yates III, et al., in that Spencer also does not disclose or suggest binding patterns generated by contacting a microarray of antibodies with a cell lysate. The Office Action states (page 9) that Spencer discloses the evaluation of binding patterns to identify cell lysates involved in inflammatory conditions. Applicants disagree. Applicants assert that Spencer et al. does not teach the use of cell lysates, binding patterns generated by cell lysates contacted with antibodies, and in particular, binding patterns generated by cell lysates contacted with a microarray of antibodies.

Thus, Claims 76-79 and 84 are nonobvious for the same reason that claim 18 is nonobvious, and Applicants respectfully request that the rejection of Claims 76-79 and 84 under 35 U.S.C. §103(a) be removed.

Conclusion

Applicants respectfully assert that upon entry of the present Amendment, the pending application is now in condition for allowance. Prompt and favorable consideration of this Amendment and Reply is therefore respectfully requested.

Respectfully submitted,

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